

Original Articles. aRECENT OBSERVATIONS ON THE FUNCTIONS OF THE THYROID GLAND; AND THE RELATION OF ITS ENLARGEMENT TO GRAVES'S DISEASE; ALSO REMARKS ON THE THERAPEUTIC USE OF SHEEP'S THYROID AND OF OTHER ORGANIC EXTRACTS.<sup>1</sup>

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THE object of this paper is to call attention to the present state of our knowledge as to some of the functions of the thyroid gland, and certain disturbances of nutrition due to its atrophy; and as to the relation of goitre to the nervous symptoms met with in Graves's disease and analogous states. I shall also speak of the therapeutic action of thyroid extracts in conditions other than myxœdema, and as to the use of some other organic extracts as therapeutic agents.

The dramatic history of the discovery of the relation of thyroid disease to myxœdema, cachexia strumiprivi, cretinism, and the so-called fetal rickets, is now, in its broad outlines, familiar to every physician, so thoroughly has public attention been aroused by the developments of the past few years. As long ago as 1856, Schiff had noticed the fatal effect of thyroidectomy in dogs; and even earlier than this Sir Astley Cooper and one or two other physiologists had made a few experiments in the same line, with varying results. In 1856 Curling described a few cases of sporadic cretinism as occurring in England; and in 1871 Dr. Hilton Fagge described others, and noted that they were characterized by atrophy of the thyroid. In 1874 Sir William Gull read his paper on "The Cretinoid State in Women"; and two years later, Dr. Ord gave a full description of myxœdema, and christened the symptom complex with its present name. He also remarked on the clinical relationship between these cases and those which had been described by Curling and Fagge, and noted that the atrophy of the thyroid made a pathological bond between them.

In 1884 came the remarkable observations of Reverdin, of Geneva, and Kocher, of Berne, who found that the thyroidectomy with which their experience in the goitrous districts of Switzerland had made them familiar, was often followed by a strange cachexia. Kocher at first thought this to be due to laryngeal asphyxia, but Reverdin a few months later recognized it as essentially identical with myxœdema. The flood-gates of physiological research were then opened, and a mass of observations began to pour in, which I have no space even to summarize.<sup>2</sup> Dr. Felix Semon, recognizing the extreme interest of the new discoveries, at once proposed the appointment of a commission of inquiry from the Clinical Society of London, the report of whose labors, finally published as a separate volume in 1888, will always be referred to as a treasure-house of facts upon this subject.

Even before the publication of this report, came the scarcely less valuable review by our own colleagues, Drs. Hun and Prudden, based on one hundred and fifty cases, and giving the details of two thorough and important autopsies. Finally, in the winter of 1891—

1892, Mr. Horsley, of London, whose name is identified with the best original research with regard to this matter, published in Virchow's *Denkschrift* and in the *British Medical Journal* (January, 1892), a comprehensive and masterly analysis of all the facts which were at our disposal up to that time, relating to the physiology of the thyroid.

Most of Horsley's conclusions have been confirmed by subsequent research; and it is now accepted by every one that the thyroid is an organ of immense importance for nutrition. A few of his views will, however, now bear revision; and a few important discoveries are to be added.

The history of the therapeutics of myxœdema was sketched anew by Dr. F. C. Shattuck at a recent meeting of the Medical Improvement Society; and I have nothing to add to his interesting remarks except to call attention to the fact that many cases of cretinism have been greatly benefited by thyroid feeding, even those where the disease had existed up to adult life. Two or three of these cases have been under the care of Dr. Osler,<sup>3</sup> of Baltimore, to whom we also owe an investigation into the frequency of sporadic cretinism in America, showing that it is a disease of rare occurrence among us.

It is probable that the thyroid is not, as Horsley thought it was, a hæmopoietic organ of real significance (Gibson<sup>4</sup> and others, and among recent observers, De Quervain<sup>5</sup>).

It is practically certain that the functions of the thyroid are not related to those of the spleen (De Quervain<sup>6</sup>). Later observations have indeed made it more and more probable that it is not safe to regard secondary enlargement of an organ following thyroidectomy as a sign of compensatory activity. This is especially important as regards the pituitary body, since this is probably or possibly related to the thyroid in function. It does frequently enlarge after removal of the thyroid and so does the thyroid sometimes enlarge after removal of the pituitary body; but Vassale and Sacchi,<sup>7</sup> who have been most successful experimenters with regard to the pituitary body, do not believe that the enlargement or the increase of colloid which accompanies it, necessarily means an increase of functional activity.

The interesting experiments by Breisacher [v. Horsley] with regard to the action of animal food in increasing the cachexia from removal of the thyroid have been confirmed, with slight modifications, by De Quervain,<sup>8</sup> in a very recent research.

This latter observer was unable to confirm the statement of Rogowitsch, Capobianco, and others<sup>9</sup> that constant demonstrable changes occur in the central nervous system after thyroidectomy.

It is not impossible that a repetition of the fatigue experiments of Professor Hodge, of Clarke University, would show that anatomical changes could be more easily induced in animals suffering from cachexia than in normal animals, and that, for this reason, anatomical changes would sometimes be present which at other times were not found. Pisenti<sup>10</sup> has recently observed

<sup>3</sup> Transactions of the Association of American Physicians, 1893.<sup>4</sup> British Medical Journal, 1893, i, p. 14.<sup>5</sup> Virchow's Archiv, 1893, Bd. 133, Heft 3.<sup>6</sup> See also Gley and other authors cited by him in the Arch. de Phys. n. et p., 1894, p. 207.<sup>7</sup> Arch. Ital. de Biol., 1893, t. xviii, p. 385.<sup>8</sup> Virchow's Archiv, 1893, Bd. 133, Heft 3.<sup>9</sup> See a paper by the writer, on cases of myxœdema, etc., in the American Journal of Medical Sciences for September, 1893.<sup>10</sup> Cited by Gley, Arch. de Phys. n. et p., 1894, p. 187.<sup>1</sup> Read before the Section for Clinical Medicine, Pathology and Hygiene of the Suffolk District Medical Society at the meeting, December 20th.<sup>2</sup> See a review, with original observations, by Dr. F. P. Kinnicut, New York Medical Record, xlv, p. 449.

the formation of small cavities, apparently of vascular origin, in the spinal cord of dogs who had survived thyroidectomy for a number of months.

The thyroid gland is found in all vertebrate animals.<sup>11</sup> It is formed by an invagination of the pharyngeal wall, and is believed by most embryologists to serve as a digestive gland, even in the lowest animals where it exists. I mention this point because a recent writer<sup>12</sup> has proposed the view that its functions are, in a broad sense, respiratory, and that this is indicated by its anatomical relations to the branchial clefts. It is supposed by him that its secretion in some way assists the oxygenation of the tissues. I am not able to say whether there is any real foundation for this theory or not, but Poehl<sup>13</sup> who has for several years been studying the chemistry and physiology of spermin, finds that this, too, has a powerful influence on oxidation, so that it is a constituent, not only of Brown-Séquard's testicular emulsion, but also of many glands and organs, and among them the thyroid.

The gland shows itself at an early period in the human embryo and, according to Horsley, it probably begins its secretory functions by the sixth or seventh month of foetal life. It is not known upon what principle the efficiency of the secretion depends; and the fact that it remains active after it has passed through the walls of the stomach, as well as after precipitation by alcohol, has not as yet cleared up the mystery, though it indicates that the active principle is a sort of ferment. The adult gland is made up of spaces containing colloid material and lined with epithelium. It is, however, doubtful whether the colloid is more than a vehicle for some more active agent. Certainly its chemical structure may change somewhat without its efficiency being destroyed. It has been clearly shown that when the gland is injured<sup>14</sup> or undergoes such changes as are seen in Graves's disease and even in phthisis<sup>15</sup> there is a strong tendency to a modification of the gland-structure, with arborescent arrangement of the tissue, higher, cubical epithelium and without colloid.<sup>16</sup> Yet myxœdema does not necessarily or even usually come on under these circumstances.

We cannot say with confidence that the gland thus altered remains in all respects as efficient as before, but even a very small part of an altered goitre is enough to ward off cachexia of serious amount. A number of cases are on record, one of which was observed by myself, where goitre with nervous symptoms passed over into myxœdema. It is a curious fact that the outbreak of the myxœdema, in my case, was attended by an enlargement and hardening of the altered thyroid, and that these peculiarities diminished during improvement, and increased again during a relapse.

Greenfield,<sup>17</sup> who has recently studied the subject, regards this tendency of the gland to change its structure in Graves's disease as an evidence of increased glandular activity in that affection. But in view of

<sup>11</sup> See W. K. Brooks, Johns Hopkins Bulletin, May, 1893.

<sup>12</sup> Andriezen: British Medical Journal, 1893, ii, p. 678.

<sup>13</sup> Berl. Kl. W. schr. 1893, No. 36.

<sup>14</sup> Halstead and Welch: Discussion on Myxœdema, Transactions Association of American Physicians, 1893.

Canizzero: Deutsche Med. Woch., 1892, p. 184.

<sup>15</sup> Defaucamberge, cited by Horsley, loc. cit.

<sup>16</sup> Greenfield (British Medical Journal, December 9, 1893) says that the secretion in exophthalmic goitre sometimes becomes mucinoid in character. He assumes that the disappearance of the colloid is due to more active absorption accompanying active secretion.

Putnam: The Treatment of Graves's Disease by Thyroidectomy, Journal of Nervous and Mental Diseases, December, 1892.

<sup>17</sup> Greenfield: British Medical Journal, December 9, 1893. See also Stewart and Gibson: British Medical Journal, 1893, ii, p. 676.

the fact that a very similar, if not exactly the same change occurs as a result of injury and disease (phthisis) the assumption cannot be accepted as certain. The fact that this change occurs after removal of part of the gland (Halstead) suggests that it means increased activity, but in Canizzero's experiments the gland was injured but not mutilated, yet a similar change occurred.

Another fact, which is important in this same connection, is the following: It was at first thought that rabbits were less susceptible than the carnivorous animals to the bad effects of thyroidectomy; but the researches of Gley showed that their survival after operation was due to the fact that in these animals (and, as it seems, in many others as well), besides the main body of the gland, accessory glands or "glandules" are present which had commonly been overlooked when the main body of the gland was removed. The literature of the "glandules" is already a large one, and I will here refer to only one point concerning them. These glandules have an embryonic structure; and although they grow larger after removal of the thyroid and to some extent seem to ward off the threatening cachexia, yet their structure does not necessarily change to that of the adult gland.<sup>18</sup>

If this observation is correct, the statement which has been made that the embryonic nodules found even in the adult human thyroid (Wölfler) develop under certain conditions into a more highly differentiated structure, may need revision.

Although it has been proved that the myxœdematous cachexia does not occur after partial thyroidectomy, provided about one-quarter of the gland is left behind, yet it is not to be assumed that even this incomplete removal of the gland is of indifference as regards the nutrition of the organs and tissues of the body. This is a subject of practical interest, and some important experimental evidence has been brought forward in regard to it since Horsley's paper was written.

It has been found that the preservation of the glandules of Gley, though it usually prevents the worst forms of cachexia, does not prevent the gradual development of a series of changes affecting the bones, the skin, the ovaries, and many other organs, especially if the animals operated on are young (Hofmeister,<sup>19</sup> De Quervain). Gley and Rochon-Duvigneaud<sup>20</sup> have recently studied with care a series of changes occurring in the eye, under these same conditions. The practical question is this, To what extent must the thyroid be mutilated, or atrophied, or diseased before some of the nutritive effects due to lack of its influence begin to make their appearance? A partial answer to this question is perhaps furnished by the fact that there are disturbances in nutrition, not identical with myxœdema but presenting one or another symptom analogous to those met with in that disease, for which thyroid treatment seems to be useful. It is needless to say that this reasoning should be used only with caution, and that no positive conclusions can be drawn as to the real value of these preparations, either as means of treatment or as pointing to a deficiency of the normal thyroid secretion.

The first person to use the thyroid of animals for other affections than myxœdema, so far as I know, was Dr. Barron of Liverpool, who, noting the fact which must have impressed every one, that patients

<sup>18</sup> See discussion between Gley and Moussu, Comptes Rendus, Société de Biologie, 1893.

<sup>19</sup> Fortschritte der Med., 1892, p. 81.

<sup>20</sup> Arch. de Phys. n. et p., 1894, p. 101.

recovering from myxœdema frequently lose weight with extreme rapidity, the loss going even beyond the limit of health in some cases, suggested the employment of thyroids in ordinary obesity. I am not aware whether he has continued his investigations or not, but in a private letter, received in May, 1893, he stated that he had used the treatment in five cases, and in three of them with marked effect.

Acting on this suggestion, I have tried the same treatment in several cases during the past year, with the following results: One patient lost 33 pounds in three months, falling from 270 to 237, but here the influence of the treatment seemed to cease. When it was suspended for a month he regained seven pounds, which he again lost on resuming the treatment, but I have not been able to reduce his weight below 237 pounds even by giving fifteen grains of the thyroid daily. No change was made in his diet or habits. His general health showed a marked gain during the thyroid treatment.

A female patient, treated by Dr. Coggesball, at the Boston Dispensary, lost 47 pounds in four months.

On the other hand, a female patient of my brother, Dr. C. P. Putnam, who weighed 240 pounds at the beginning of the treatment, after losing five pounds the first week, seemed to be no longer affected; and I have had three or four other patients in whom only a temporary loss of weight (up to fourteen pounds in one case), or none at all, has occurred. Possibly, larger doses might have had more effect.

It seems clear from the many experiments which have now been tried, that healthy persons are not so easily affected in an injurious way by the thyroid treatment, though certain symptoms, especially an increase in the pulse-rate, occur with considerable regularity.<sup>21</sup> It would seem that we do not yet know the conditions which make one person a suitable subject for this treatment and another not so. It will be interesting if it turns out that the loss of weight, even when it occurs, cannot be made to go on indefinitely.

Another therapeutic use of thyroid preparations is in the treatment of diseases of the skin, especially in psoriasis, eczema, and xeroderma. The first of these cases was brought forward by Dr. Byrom Bramwell at the annual meeting of the British Medical Association, August, 1893;<sup>22</sup> and the photographs which he there showed were very impressive. Unfortunately, one of these cases afterwards relapsed, and not all the more recent observers have been equally successful, even in their primary results. Dr. Hartley<sup>23</sup> obtained favorable effects, and Dr. Arthur T. Davis<sup>24</sup> likewise, while Talfourd Jones<sup>25</sup> experimented on a case of psoriasis, with the apparent result of making the disease spread. Lesley Phillips<sup>26</sup> obtained improvement in a case of xeroderma but none in three cases of psoriasis and one of eczema. It may turn out that the remedy is useful only in a certain class of these cases, or that it acts indirectly by exerting a psychical influence.

The history of therapeutics shows that new remedies sometimes have a mysteriously good effect. It is highly probable that these effects do not occur through mere coincidence, and are not wholly to be explained

by the assumption that the most favorable results are the first to be made public. The researches of the past few years have taught us that psychical influences can be counted upon to affect the nutrition to a degree formerly not dreamed of, and the effects of the new remedies must be studied anew from this standpoint. It is noteworthy that eczema has been favorably influenced by hypnotism pure and simple, and that good results have followed injections of testicular fluid in eczema, leucoderma, ichthyosis.<sup>27</sup> Eccles<sup>28</sup> has used spermin in similar cases with favorable effects.

Finally, Vermebren, of Copenhagen, has made an interesting series of experiments with thyroid preparation, in various conditions of impaired nutrition, with the special view of testing their action on some of the changes of old age.<sup>29</sup> He first treated three cases of myxœdema with thyroids, and gave also measured quantities of food, and followed the urea excretion. This increased in the course of the first five days in all three cases, finally reaching twice or three times the amount noted for the period before the experiments were begun. In one case it then remained at the maximal point during the continuance of the treatment, so long as the experiments lasted. In the other two cases it fell rapidly, after the first rise, but in one of these it rose again at a later time. A small part of this increased excretion of urea was found to be probably referable to an increased absorption from the intestine. The patients also lost fat largely, but the rate of loss was not estimated.

The non-myxœdematous patients experimented on were: (1) A boy of seven years, with fracture of the tibia; (2) a girl of seven, greatly emaciated and perhaps infected with tuberculosis; (3) a woman of twenty-eight, with chlorosis and gastric catarrh; (4) a man of fifty-two, but very old for his years, with chronic alcoholism; (5) a man of sixty, also old for his years, with chronic bronchitis; (6) a man of sixty-two, with varicose ulceration of the leg.

The study of the urinary excretion seemed to the author to warrant the conclusion that in the cases of the young persons the only positive effect of the thyroid treatment was a moderate diuresis, while with the elderly patients changes occurred like those seen in myxœdema, though to a less degree. It is obvious that more experiments are needed before this conclusion can be accepted as of general significance; but it is certain that slight degrees of myxœdema occurring in the period of involution are liable to be overlooked. I have recently observed and shown a patient<sup>30</sup> whose case was perfectly clear on close study, but whose appearance alone would not have attracted notice as abnormal. The case of an elderly gentleman recently described by Dr. F. C. Shattuck, is important in this connection, and not less so for illustrating the liability to the persistence of the ill-effects of thyroid medication, — when such effects occur at all — long after the treatment has been stopped.

#### THERAPEUTIC ACTION OF OTHER ORGANIC EXTRACTS.

It was impossible that the wonderful discoveries with regard to the effects of thyroid extracts in myx-

<sup>27</sup> Monnet: *Journal of Cutaneous and Genito-Urinary Diseases*, vol. ix, 1893.

<sup>28</sup> *British Medical Journal*, 1893, vol. ii, 474.

<sup>29</sup> *Stoffwechseluntersuchungen nach Behandlung mit Glandula Thyroidea an Individuen mit u. ohne Myxœdema*, Deutsche Med. Woch., 1894. See also, in this connection, Ord and White, *British Medical Journal*, July 29 and December 9, 1893.

<sup>30</sup> *Boston Medical and Surgical Journal (Society for Medical Improvement)*, 1894.

<sup>21</sup> See, among other papers, Greenfield's Bradshaw Lecture, *British Medical Journal*, December 9, 1893.

<sup>22</sup> *British Medical Journal*.

<sup>23</sup> *Ibid.*, 1894, vol. ii, p. 764.

<sup>24</sup> *Ibid.*, p. 474.

<sup>25</sup> *Ibid.*, 1894, ii.

<sup>26</sup> *Ibid.*, November, 1893.

œdema should have failed to renew the interest in the use of the other organic extracts (of testicle, brain, spinal cord, etc.) suggested by Brown-Séquard and D'Arsonval,<sup>81</sup> by Babes,<sup>82</sup> and by Althaus.<sup>83</sup>

The subject is large enough for a whole evening's discussion, and I cannot pretend to do it justice here. The many observers who have obtained good results from these remedies bring forward an astounding and impressive array of facts in support of their view. Poebl<sup>84</sup> shows that similar results may be obtained with his *spermin*, a definite compound obtained from the testicles and the ovaries, and from other glands as well, and adduces evidence that a part of these results are due to increased oxidation occurring under special conditions. It is obvious that all these observations are not to be treated with ridicule, and especially not from an *a priori* standpoint.

What one may and must say, however, is this, that the case for testiculine and cerebrine and myeline in neurasthenia and tabes, and the like, rests on a wholly different basis from that of the case for the use of thyroid in myxœdema. It is not as if we were attempting to cure by injections of spermatic fluid a series of clear and invariable results following castration, though this would be a highly interesting and important experiment. It is a much more difficult matter to decide whether the improvement which takes place in various diseases, even diseases characterized by gross structural changes, like locomotor ataxia, is due to the remedy which has been given.

Explain the fact as we may, the value of all but the clearest therapeutic experiments is enormously vitiated by the fact that mental influences which we cannot gauge are capable of profoundly affecting the result. The powerful phantom of suggestion stands behind the physician's chair, unseen both by him and by the patient, and the influence of the unwelcome intruder is often increased by the very efforts that are made to exorcise him. Althaus, the latest experimenter, recognizes this general fact, but thinks that his observations are free from suspicion on account of the intelligence and mental balance of his patients, and because no attempt was made to impress their imagination. But, the very use of this reasoning indicates a failure to grasp the true significance of the discoveries of the past few years as regards the relation of psychical influences to nutrition. It is not necessary that the patient's imagination should be impressed, in order that results may be produced due to what — for lack of a better name — we must call "suggestion." In hypnotic suggestion the imagination can hardly be said to enter as a factor at all; and even in the many forms of waking suggestion, there is often no conscious stimulation of the imagination. It is, of course, not always easy to say why one drug or treatment should have a markedly greater effect than another; but two causes suggest themselves as often effective. One is the influence of the physician's own feeling of hope or interest, which he may try in vain to conceal,<sup>85</sup> and by which the patient may easily be impressed without being himself aware of the fact; the other is the influence of an interest previously stored in the patient's

mind by bearing or reading of the remedy or the method, but perhaps wholly forgotten so far as conscious memory is concerned. The phenomena of "crystal vision," and a host of kindred facts show how potent such "forgotten" cerebral impressions may continue to be. Within certain limits these influences would be all the more active if the patient was intelligent and a person of wide reading and quick instincts of observation.

The admissibility, to say the least, of this explanation of the action of injections of organic extracts is shown by the success which has attended the substitution, under certain precautions, of inert fluids for the testicular or nerve extracts. A large number of control experiments of this sort have been made by other observers,<sup>86</sup> and one or two by myself.

One general fact is noteworthy in connection with this branch of the subject, and that is that cures of tabes or locomotor ataxia are perhaps more numerous than any others except neurasthenia. It is, now, well known — in spite of Charcot's "Quand on guérira le tabes it fera cbaud"<sup>87</sup> — that amelioration of some of the symptoms of locomotor ataxia has been brought about, here and there, by several different remedies, such as suspension, injections of phosphate of sodium, and by hypnotism (Moll) as well as by the organic extracts. Moreover, it was noticed long ago, by Westphal and his colleagues, that in cases when the lesions of tabes were combined with those of cerebral degeneration, the ataxia of motion was apt to be much less prominent than where the mental condition was sound. Finally, it is well known that the symptom of pain is pre-eminently susceptible to hypnotic and to waking suggestion; and that persons in a state of somnambulism exhibit an unusual fineness of muscular sense, or sense of position.

It is admissible, I think (though, of course, not obligatory), to read the significance of these facts as follows: that patients with locomotor ataxia are better subjects for psychical treatment than patients with many other analogous forms of disease, because (1) their pain is susceptible of relief in this way, and (2) the aggravation of their ataxia coming from misdirected conscious efforts can be relieved by influences which shunt out the consciousness of their disability in a measure. Perhaps the relief of these symptoms tends also towards a real nutritional improvement in the nerve-centres. Certainly, the reverse is often true, namely, that organic lesions are unfavorably affected by the influence of the symptoms to which they give rise.

Locomotor ataxia seems, again, to be one of those affections where the symptoms may subside in spite of the persistence of the lesions, provided (probably) that the disease is not actually progressing. The important case, with autopsy, by F. Schultze<sup>88</sup> published in 1882, affords strong evidence for this view.

My own experience with the testicular and cerebral extracts extended over about a year, during which time I used the injections in a good many cases, but only in nine or ten with a persistence to justify a use of them for clinical inferences. These cases comprise three of locomotor ataxia, and six of what I may call, with sufficient accuracy, neurasthenia. Besides these

<sup>81</sup> Arch. Physiol. norm. et path., for the past three years; Comptes Rendus Soc. de Biol.; British Medical Journal, June, 1893, etc.

<sup>82</sup> Constantin Paul, Soc. de Thérapeutique, Session of February 24, 1892.

<sup>83</sup> Lancet, December 2, 1893.

<sup>84</sup> Berl. klin. Woch., 1891 and 1893.

<sup>85</sup> The observations on "muscle-reading" should be borne in mind in this connection.

<sup>86</sup> Massalongo: Le Iniezioni di Liquidi Testic. di Brown-Séquard, etc., un Nuovo Capitolo di Therapeutica Suggestiva. Riforma Med., February, 1893.

<sup>87</sup> Stockwell: Medical News, August 26, 1893.

<sup>88</sup> Quoted by Althaus, loc. cit.

<sup>89</sup> Zur Frage v.d. Heilbarkeit der Tabes, Arch. für Psych. u. N. heilk., vol. xii, p. 232.

I have the notes of the treatment of a case of chronic myelitis which Dr. Coggeshall kindly allows me to report with the rest. I have also, as a control experiment, treated, for about a month, a case of locomotor ataxia by the injection of a simple mixture of glycerine and water. During part of the time I used testicular fluid obtained from Paris through the kindness of Dr. Brown-Séguard, but the greater part of the extracts were made at the Pasteur Institute of New York. The habitual dose was about two or three grammes. In their most recent publications Brown-Séguard and D'Arsonval advocate a dose larger than this.

The summary of the results of my own experience is as follows: In one of the tabetic cases an apparent improvement was shown, not only in a most gratifying general gain (by relief from pains and increase in strength), but also by the apparent cure of one of the gastric crises. The subsequent history of this patient is, however, very significant. At a later period injections of glycerine and water seemed, also, to help him very much, but after this even testiculine failed to prevent a rapid prostration. Another tabetic patient who was treated with testiculine for about a year, with gain as regards relief of pain and general sense of well-being, was attacked with tubercular laryngitis towards the end of this period, and shortly afterward died. This is noteworthy because Dr. Brown-Séguard has claimed that tuberculosis also is favorably influenced by the remedy. The third patient thought his pain relieved, but there was no marked or permanent improvement in the course of two or three months of treatment.

In Dr. Coggeshall's case of chronic myelitis, the patient received three injections of three to four grammes each, of testiculine, every week, and at the end of seven weeks had gained greatly in every respect. In this case there was a history of syphilitic infection fifteen years before, and the final symptoms were of nine years' duration. Under the injections the improvement began at the end of two weeks. After five weeks of treatment there was a marked gain in power of muscular endurance, a gain of weight of four pounds, an increase of half an inch in the girth of the calves, and of one inch in the girth of the thighs. The grasp, as measured by the dynamometer, increased from 60 to 110. Unfortunately, even while the treatment was still in progress, the patient began to relapse, and had soon gone back nearly or quite to his earlier state.

As an offset to these cases, I will briefly report the case of tabes treated by injections of glycerine and water. The patient was a married woman about thirty years old, and there was reason to think that she had been inoculated with syphilis by her husband. The tabetic symptoms, which were of several years' standing, consisted in severe characteristic pains; ataxia of both arms and legs; Argyle-Robertson pupils, with irregularity in outline; loss of the knee-jerk; and impairment of control of the bladder. I had intended to treat her with testicular fluid, and gave one injection for that purpose. At the next visit, however, happening to be out of the fluid, and not wishing to disappoint her, I gave an injection of glycerine and water. At the next visit she was better, and so I thought I would continue the glycerine and water, *experimenti causâ*. This is now two months ago, and she has continued steadily to improve in most respects. The ataxia of the hands is no better, but the gait has improved so much that, whereas at first she had to bring

a companion with her, she now comes alone. The pains, also, have left her, and in her general health and feeling there is a distinct gain.<sup>89</sup>

Of the six neurasthenic patients who remained under treatment long enough to make their histories of value, three were men, three women.

Of the men, one was a gentleman past middle life, eminent for scientific training and powers of observation, who had been for some little time in a nervously debilitated condition, owing to stress of work and other causes. The injections were begun by Brown-Séguard, and continued for a time by me, eventually by himself. The treatment was marked by steady improvement, and ended in complete recovery.

The second case was that of a typically neurasthenic patient, an intelligent physician, rather below middle life, and of good nutrition. The symptoms consisted mainly in an incapacity for application without great mental effort and distress, so that steady work, especially of a literary kind, was well-nigh impossible. Temporary improvement of a very marked sort occurred during the first week of the treatment, and recurred to some extent when the treatment was resumed after an interval of cessation. In the end, however, in spite of thorough and persistent efforts, no permanent benefit was obtained.

With both of these cases one interesting symptom showed itself a few times, when the treatment was first begun, namely, a tendency to erections on the night following the injections. This has been noted also by other observers, but is not regarded as due to the specific character of the fluid, and does not, it would seem, imply that the treatment is especially effective against impotence. In one case of this sort, of purely neurasthenic character, a few injections had no effect.

The third case was that of a young man in a typically neurasthenic state, with morbid fears and marked loss of endurance, due, apparently, to sunstroke. The improvement was steady, but as it had begun before the injections were used, under the influence of encouragement, electricity, etc., and continued after the cessation of the injections at the same rate as before, I did not feel that a large share of the result was to be ascribed to them.

The first of the female cases was that of a young girl with infrequent attacks of epilepsy, and great debility. The improvement during the use of the injections was very great, as regards the debility. The fits were too infrequent to warrant conclusions about them.

The second case was that of a lady past middle life, in a condition of slight mental deterioration of unknown origin. The use of the injections, which were faithfully given for many weeks, afforded her encouragement, but brought no real improvement.

The third patient was a woman with mild hysteria, or neurasthenia with hysteroid symptoms of sensory character. Not many injections were given, but after each one she felt distinctly better. In this case the gain was undoubted, but a similar gain and one equally great followed each of many applications of static electricity, and I was inclined to attribute it in both cases to the encouragement attendant on systematic treatment.

I do not maintain that these few observations are in the least conclusive in either direction; but while it is

<sup>89</sup> Some months have passed since this statement was written, but I have not seen the patient this winter, and do not know her later history.

true that all which has been claimed for the organic extracts may have been claimed with justice, yet it should not be forgotten that the claims of hypnotism in similar lines are equally far-reaching, and that what hypnotic suggestion can accomplish it is also possible for waking suggestion to accomplish, under sufficiently favorable conditions.

I will now ask your attention to the consideration of another class of affections associated with diseases of the thyroid, those namely, of which Graves's disease may be taken as an extreme type.

This subject is not yet ripe enough for definite conclusions; and a discussion of the points involved, to be adequate, would necessarily be long. I shall therefore content myself with referring to a few prominent considerations.

In the first place, What is the probable relationship of goitre to the other symptoms of Graves's disease? The following answers, no one of which seem to me wholly satisfactory, have been offered in reply to this question:

(a) Graves's disease is made up of a collection of conditions, part of which are due to the irritation of nerves ramifying in the enlarged thyroid or lying near it, while part are due to an altered thyroid secretion, which acts as a poison. The cardiac symptoms may also be in part explained by disturbance of respiration, as in ordinary goitre.

(b) The whole symptom-complex of Graves's disease is of toxic origin, and due, directly or indirectly, to an increased amount of thyroid secretion or an alteration of its quality.

(c) Thyroid enlargement has no causal relation to the other symptoms of Graves's disease, but like them is due to a disturbance of the nervous system, the exact seat of which is unknown, but which probably consists mainly in a disturbance of some of the functions of the medulla-oblongata.

(d) Finally, the enlargement of the thyroid may be partly a cause, partly a symptom of the Graves's disease complex.

Without attempting to take a positive position in favor of either of these views I will call your attention to a few salient facts.

(1) Quite a large number of cases have now been published in which the partial removal of the enlarged thyroid has led to great improvement and even cure of Graves's disease. I have recently collected fifty-one cases of this sort, in all but a few of which, substantial improvement was obtained by operation. Since I made my collection still others have been reported.<sup>40</sup> At the same time, the results have not been uniformly good. A case which I have carefully followed was operated on by Dr. J. C. Warren nearly a year ago, and of late even the remnant of the thyroid has nearly disappeared. Nevertheless, the improvement in the patient's condition, though satisfactory in some respects, has not been marked by any permanent change in the exophthalmus or the tachycardia.

(2) Although typical Graves's disease is not common in goitrous districts, yet it is common for patients with ordinary goitre to suffer from some of the symptoms of Graves's disease, especially dyspnoea, palpitation and dysphagia. (Mueller,<sup>41</sup> Maude, Wette,<sup>42</sup>

Schranz,<sup>43</sup> etc.) It is in fact for these symptoms that patients with goitre usually present themselves for operation, and it is not difficult to give a fairly satisfactory explanation (Wette) of the way in which the enlargement of the thyroid might lead to them. The following conditions are often met with: (a) Patients with large thyroids, without other symptoms of any kind; (b) patients with large thyroids and symptoms referable to the respiration and pulse. Occasionally slowing of the pulse is seen (Wette); (c) patients with these symptoms, and in addition, perhaps, exophthalmus and some general nervous disturbance; (d) the same, with the addition and other disturbances frequently met with in connection with Graves's disease.

(3) Some of the symptoms of Graves's disease are occasionally excited by some cause apparently wholly independent of the thyroid. This is true, for example, of exophthalmus, which seems to be sometimes due to disease in the nasal cavity and to sympathetic irritation.

(4) Graves's disease sometimes comes on with great rapidity under emotional excitement, so rapidly that it hardly seems possible that the thyroid secretion should have become increased, although it might have become altered in quality.

(5) There is no good reason for characterizing Graves's disease as a cachexia.

(6) The Graves's disease complex strongly suggests the symptoms met with in conditions of extreme excitement, as in fear or in anger, that is, it occurs as a quasi-physiological complex.

(7) Operations on goitres are sometimes followed by sudden death or by extreme disturbance of the heart and respiration; and no satisfactory explanation for this has yet been given, though several of great interest and importance have been suggested. One that has not been suggested, so far as I know, and which may be worth considering is, that if a large amount of thyroid secretion is poured out from the cut surface of the gland into an open wound it must be rapidly absorbed. Against this view, however, is the fact that these serious symptoms do not always occur.

(8) Improvement may be brought about in cases of Graves's disease by various influences, both general and reflex, tending to quiet a disturbed vascular excitement of the gland or of the heart.

(9) The symptoms of Graves's disease bear a certain resemblance to the nervous symptoms of the first stage of cachexia strumipriva. But this resemblance is not a close one, nor is the contrast which has been suggested as between myxœdema and Graves's disease, more than superficial.

(10) Although the histological characters of the enlarged gland in Graves's disease are altered, and the secretion of colloid is apparently deficient, yet the removal of the greater part of such a gland does not lead to myxœdema.

(11) On the other hand, myxœdema occasionally follows Graves's disease in the same patient, or the two diseases are seen in different members of the same family; and in the same family ordinary goitre may be met with.

We have no right to assume that goitre was the original cause of the symptoms which are cured through its removal.

The recent view that the symptoms of Graves's

<sup>40</sup> Mainly collected by Mebius (Schmidt's Jahrb., 1893). See also Maude: Lancet, 1893, ii; Freiberg: Medical News, August 26, 1893.

<sup>41</sup> Deutsches Arch. für klin. Med., 1893.

<sup>42</sup> Arch. für klin. Chir., 1892, vol. 44.

<sup>43</sup> Ibid., 1886, vol. 34.

disease are due to excess of thyroid secretion, although supported by some evidence, has not been fully established, and is strongly controverted by a recent case in which the disease was cured by sheep thyroid taken by the stomach.<sup>44</sup>

### THREE CASES OF SALPINGITIS OF UNUSUAL EXTENT.<sup>1</sup>

BY MAURICE H. RICHARDSON, M.D.

- I. DOUBLE PYO-SALPINX OF TUBERCULAR ORIGIN; REMOVAL; RECOVERY.
- II. DOUBLE PYO-SALPINX, PROBABLY TUBERCULAR; REMOVAL; LOCAL PERITONITIS; RECOVERY.
- III. DOUBLE PYO-SALPINX OF SEPTIC ORIGIN; REMOVAL; DEATH.

THE following cases are unusual because of the extraordinary size of the tubes. They are interesting also from their etiology. In the first case the question of diagnosis was a conspicuous feature; the tumors, from their size and apparent solidity, with their intimate connection with the uterus, having deceived every one who examined them. Apparently the growth was a lobulated fibroid. The diagnosis seemed so clear that a sound was not put into the uterus; yet it does not follow that because a uterine sound does not enter an abnormal distance that the uterus is not enlarged. In the second case the diagnosis was easy. The source of the trouble, however, was not so clear. It was impossible to exclude a tubercular element in this case. The possibility of an infection through the uterus was also considered. Whatever may have been the cause in this instance, the great size of the tubes, their outline and their situation made the case one of unusual interest. In the third case a history of a direct infection through the vagina and uterus made the etiology more positive. The methods used and their results justify certain conclusions of value to me in the future management of similar cases.

CASE I. N. Q., aged twenty-four, single. Entered the Massachusetts General Hospital July 5, 1892. There was a family history of consumption. The patient has never been sick. One year ago she began to have pain in the back, which of late has been less severe than at the first. For some time she has noticed a swelling in the lower abdomen on the right side. Of late the pains have been referred to the thighs and have been sharp and shooting. Catamenia regular until last month, when they were absent. She had always had dysmenorrhœa. There has been a slight vaginal discharge. She has lost thirty pounds in weight in the last year. Her appetite is good. Urine normal. She is not confined to the bed.

Below the umbilicus the abdomen was enlarged, and contained a mass about the size of a six months' foetus, with two prominent tumors. The mass of both tumors was somewhat to the right of the median line and was slightly tender and movable. The uterus moved with the movements of the tumor. The uterine sound was not passed. A large mass could be felt in the posterior cul-de-sac. She was examined by several of the staff, and the diagnosis of a uterine fibroid was made. This case was carefully studied until the 15th of July, when a median laparotomy was performed. As soon as the abdominal pressure was

<sup>1</sup> Read before the Obstetrical Society of Boston, December 9, 1893.

<sup>44</sup> Owen: British Medical Journal, 1893, ii, p. 1211.

relieved by delivery of the tumors, both stood upright in the wound, presenting the very extraordinary appearance of two convoluted masses, perfectly symmetrical, attached one to each cornu of the uterus, like enormous spiral horns. Both tumors extended deep into the pelvis and were attached by adhesions so easily separated that the continuity of the tubal wall was not broken. The peritoneum was studded with miliary tubercles; — tubercular salpingitis was evident. The patient made an uninterrupted recovery. A small portion of the omentum was removed for microscopic examination.

Dr. Mallory's report is as follows: Nodules miliary tubercles. The tubes are eighteen and nineteen centimetres in length, circumference twenty-four centimetres each, weight *one and one-half pounds each*. Thin walls filled with thin, greenish-yellow pus; peritoneal surface studded with gray miliary tubercles.

The patient came to the hospital to have this operation performed so that she could get married. I dare say that she has carried out this intention. This case is an extraordinary one from the great size of the tumors, and is interesting from the difficulty met with in diagnosis and from the glaring error made by every one. The necessity for the operation was apparent, even with the incorrect diagnosis of fibroid. The shape of the tumors was characteristic of the large dilatations of the Fallopian tubes. The great lengthening of the tube which accompanies the increase in lumen gives a spiral shape to the tumor. This appearance was well marked in the other cases. As a rule the distal end of the tube becomes rounded and projects into the pelvis, where it becomes adherent. In the present instance the enormous double enlargement was so great that the pelvis could not hold the mass. The tumors were not so deeply attached and firmly adherent as in Cases II and III. Separation was therefore accomplished so easily that no fluid escaped.

CASE II. Massachusetts General Hospital, August 26, 1893. Eunice G., aged twenty-six, married five years ago, has always been well. One miscarriage four years ago. Catamenia have been irregular, several periods having been missed without pregnancy. Four years ago, after being sick in bed with pain in the right side, the doctor lanced an abscess in the vagina. A year later a lump was noticed in the right side of the pelvis which has lasted ever since. Two weeks before entrance, she was taken with chills, fever and great general tenderness.

General condition poor; facies "peritoneal" and anxious. Marked swelling in the lower abdomen over right tube, with increased resistance and ill-defined dulness. Great tenderness at this point; whole abdomen somewhat tender. Constitutional symptoms severe. By vagina a bulging mass was felt on both sides of the uterus, which was firmly fixed in the centre.

The question of supra-pubic operation presented itself. The fluctuating tumor felt by the vagina invited drainage in that direction; but the unsatisfactory results that follow vaginal and rectal drainage in pelvic abscesses; the brilliant recoveries which take place after abdominal section, with the immobility and sharp definition of the tumor that presented in the abdomen, decided me to take the abdominal route.

In the extensive tubal disease found in this case abdominal section is much better than vaginal drainage, in my experience. Recovery is much more rapid and

*absolutely false; even himself admitted that he had by mistake used  
they were instead of thyroid.*

complete. Moreover the mortality is no greater, considering the complications that may attend the prolonged convalescence of the latter method, the insufficiency of the drainage at times, and the not infrequent involvement of the bladder. To have seen a few women slowly waste away and die after the failure of rectal and vaginal incisions, to have seen the greatly increased dangers and difficulties of the abdominal operation after the failure of the vaginal, to have watched the progress of intestinal, vesical and other fistulæ — to have seen a few of these deplorable conditions, makes one hesitate in adopting the so-called safe operation of dependent (always septic) drainage. Not that vaginal drainage should never be employed. It can do no harm when an abscess is clearly pointing, for, by the supra-pubic, rectum drainage will have to be established, and probably vaginal also. But in conditions in which complete extirpation of the dilated tubes and their contents is possible, there is no argument of weight in favor of the vaginal, much less the rectal incision.

On the 28th of August a median incision was made, with the patient in the Trendelenberg posture. The abdominal cavity was thoroughly protected from possible extravasations by means of gauze barriers. The right tube was found to be as large as two fists, and everywhere adherent. The whole tumor was freed from its adhesions and delivered from the abdominal wound. The uterine attachment was tied close to the uterus. On the left side, also, a tumor was found — not quite so large as the one in the right. In freeing the adhesions on this side the abscess was ruptured, and at least four ounces of what seemed to be pus escaped. In spite of every precaution, the intestines were somewhat contaminated by this fluid. The tube was delivered and tied near the uterus with silk. The contents of this tumor, like that of the right, seemed to be purulent. It was greenish-yellow and odorless, thick and tenacious. The intestines that presented were carefully wiped with sterile gauze; the abdominal wound was closed without drainage.

The patient's temperature rapidly fell to the normal line, and she improved very much. In the course of a few weeks, however, she began to get hectic. A mass could be felt both by vaginal and by abdominal palpation. I was on the point of incising the posterior cul-de-sac several times. Finally, however, there was an abundant discharge of pus with a small piece of gauze from the rectum. Through this spontaneous opening the finger could be introduced into an abscess cavity situated behind the uterus. The convalescence from this time was steady, and she is now in excellent condition.

The dangers by the intra-abdominal method of treatment in cases of this kind may be very great. Safety to the patient depends upon causes beyond the control of the surgeon, if he selects this route. It is beyond human skill in many cases of this kind — in which the tubes are enormously dilated and presumably adherent, to remove the tumor without rupturing it. Notwithstanding all precautions, the extravasated fluid will contaminate the peritoneum more or less on all sides. In spite of irrigation, of wiping out with gauze, of thorough disinfection — of every thing that we can do in those instances in which the fluid contains the more septic micro-organisms — the dangers of a general and fatal peritonitis are very great. In this case, the abdominal wound was closed. We knew nothing

as to the septic or aseptic qualities of the fluid when the peritoneal cavity was sealed. We were very fortunate, therefore, that there was not a general septic peritonitis and death. The accidental presence of the gauze would have had nothing to do with the sepsis in the absence of a septic element pre-existing in the fluid, for I have often left gauze-padding much longer than this without symptoms. Unless we can demonstrate on the spot, by some of the rapid methods of staining micro-organisms, the absence of these bodies, we have no right at present to close the abdominal wound. We must give the patient the benefit of the doubt, and provide for drainage in every instance. Not that drainage is sure to prevent a general septic infection — it will not do this invariably; but if by means of tubes or of gauze, or of both, the toxic products of germs can be removed as fast as they form, the prospect of recovery is much better.

CASE III. Sarah H., aged forty-five. Boston. Admitted to the hospital October 1, 1893. Menstruation regular, slightly painful, not profuse, for thirteen years. Married twenty-seven years ago. No children. Second marriage four years ago. No children. Pregnant once at nineteen, and some sharp instrument was used to produce abortion. Has never been free from pelvic trouble since. During the last twelve years has had various disorders — pneumonia, congestion of the lungs, nervous prostration, etc. Last summer a tumor was discovered in the left ovarian region. Six weeks before entrance to the hospital, while doing her housework, during her catamenia, pain to which she had been subject off and on for years, became worse than usual, and she had to go to bed. In the course of two days an ulcer broke in the womb, and thick, greenish matter escaped. Has been in bed ever since. There have been severe spells of vomiting, lasting a day at a time. Micturition has been frequent and difficult. Yesterday and to-day has had chills and fever for the first time.

Face pale and pasty; valvular disease of the heart; abdomen very fat, and somewhat tender all over, especially above pubes and to the left, where a round mass about the size of two fists or larger, dull on percussion, could be indistinctly felt. In addition to the tumor on the left, another could be felt less distinctly on the right; both were fluctuating, and seemed unattached to the abdominal wall.

At my first examination (without ether) it seemed to me that the operation would consist simply in incision and drainage, either through the abdominal parietes, to which the tumor on the left seemed then adherent, or through the vagina, or by both routes. As soon as the patient was etherized, however, the unattached condition of the tumor on the left and the presence of another on the right could be clearly demonstrated. I therefore made the median incision, the patient having been prepared for laparotomy. The right tube was enlarged to about the size of two fists, or a little smaller; it was adherent deep in the pelvis, but not attached anteriorly. The adhesions were separated carefully, and the whole mass was delivered without rupture. A ligature was applied close to the uterus; and the whole tumor removed. There was no escape of fluid during this procedure. The left tumor, which was considerably larger than the right, was next isolated, as far as possible, by separating the recent adhesions. The undelivered extremity of the tube, pointing downwards and forwards to the left